DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Tracking Form for Applicants for New Technology Add-on Payments under the Acute Inpatient Prospective Payment System (IPPS)

1. **Technology Name**: Iotrex for brachytherapy with GliaSite® Radiation Therapy System (RTS)

2. **Manufacturer Name:** Proxima Therapeutics, Inc.

3. **Trade Brand of Technology:** GliaSite® Radiation Therapy System (RTS)

4. **Brief Description of Service or Device:**

   Iotrex is an organically bound liquid form of Iodine^{125} used in intracavitary brachytherapy with the GliaSite® Radiation Therapy System (RTS). Iotrex is a single non-encapsulated (liquid) radioactive source. The liquid is a solution of sodium 3-(125I) iodo-4-hydroxybenzenesulfonate and is used in a breakthrough approach to deliver brachytherapy for treatment of brain cancer. The delivery system for Iotrex is the GliaSite catheter. Iotrex is administered via injection through a self-sealing port into the primary lumen of the barium-impregnated catheter that leads to the balloon reservoir.

   After a malignant brain tumor has been resected, the balloon catheter (GliaSite catheter) is implanted temporarily inside the cavity. The patient is released from the hospital. After a period of 3 days to 3 weeks, the patient is readmitted. At this time, the appropriate dose (200 to 600 millicuries) of radiation is administered. Iotrex is infused into the GliaSite catheter and intracavitary radiation is delivered to the target area. The gamma radiation emitted by Iotrex is delivered directly to the margins of the tumor bed. This approach allows the physician to maximize total radiation to the target area. Because the radiation dose rapidly decreases beyond the tumor site, there is minimal damage to surrounding healthy tissue. After 3 to 7 days, the Iotrex is removed.

New Criteria

5. **Date of Food and Drug Administration (FDA) approval (or expected approval) for the device or service:**

   GliaSite® Radiation Therapy System (RTS) was approved by the FDA April 25, 2001. A copy of the FDA approval letter is attached to the application as **Exhibit C.**

(For the complete application requirements, please see the instructions at http://cms.hhs.gov/providers/hipps/10_03_application.zip**)**

Note: The information provided on this tracking form will be made publicly available.

6. **Does the technology have an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code(s) or is an application pending?**
    a. **If yes, please provide the ICD-9-CM procedure code(s) used to identify the clinical procedure(s) with which the medical service and technology is used.**

       ICD-9-CM 92.27, Implantation or insertion of radioactive element is used to identify the insertion of the radioactive brachytherapy source.

    b. **If there is no existing ICD-9-CM code that captures this new technology, please indicate whether you will be applying for a new code.**

       N/A

7. **Have you submitted an application for outpatient pass-through payments under the Medicare outpatient prospective payment system? If so, please provide the tracking number or, if it was approved, please provide the date of approval.**

   Brachytherapy solution, Iodine-125, per mCi (C2632) was determined a payable device under the HOPPS effective 1/1/03. See **Exhibit D** of the application for a copy of the Program Memorandum, Transmittal A-03-076, dated August 29, 2003.

Cost Criteria

Provide the following information to demonstrate the technology or service meets the criterion.

8. **What is the anticipated average standardized charge per case involving this new technology? For details how to standardize charges please refer to the technical appendix of the application form.**

   The anticipated standardized charge for cases mapping to DRG 007 is $48,820.

9. **What is the total estimated cost per case for the service or technology (this will include all costs involved in the case, including the cost of the service or device)? What is the cost of the technology per patient? Please provide a breakdown how the cost of the technology is calculated (i.e. Devices- breakdown of the cost of all components used in the new technology).**

   An average of two vials per patient is necessary to treat one patient using the GliaSite RTS. The current price of one vial of Iotrex is $5400 and a total patient cost for the device is $10,800. Required additional costs include two catheter trays ($390), syringe pharmacy service ($480) and solidifier for radioactive waste disposal ($195).

   The total estimated cost per case for this technology including all device related costs is $11,865 per patient.

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10. List the diagnosis-related groups (DRGs) to which cases involving this new technology will most likely be assigned.

ICD-9-CM	Description	DRG
92.27	Implantation or insertion of radioactive element	007

11. What is the anticipated volume of Medicare cases involving of this technology (by DRG)?

14,782 cases are reported for DRG 007. It is estimated that 10% of these patients will be candidates for GliaSite RTS. Based upon these estimates approximately 1,478 patients are expected to benefit from this technology in 2004.

Clinical Improvement

12. Please provide a short synopsis of the following clinical issues added to the new technology. Use the regular application to submit full details.

a. Briefly describe how the new service or technology represents a substantial clinical improvement over existing services or technologies:

Conventional Brachytherapy

Brachytherapy has historically involved the use of small, encapsulated radioactive sources (seeds) implanted short distances apart within a malignant tumor. The use of these radioactive seeds continues to be an important weapon in the armamentarium used to treat multiple tumor types (brain, breast, prostate, etc.). For example, interstitial brachytherapy is currently being used to treat brain tumors with up to 125 seeds implanted stereotactically directly into the tumor. A 7 to 16 month improvement in median survival time has been noted in patients with malignant gliomas. However, seed brachytherapy is a very complex procedure for treatment of brain tumors. Seed brachytherapy involves the invasive placement of radioactive seeds with multiple steel needles into the brain and tumor tissue. Because of the difficulty of placing multiple radiation sources, the radiation dose is frequently non-uniform with the potential for hot and cold spots. Consequently, traditional brachytherapy often requires additional surgery to remove necrotic brain tissue. The complexities and complications of using seed brachytherapy have limited its widespread use in treating brain cancer, despite studies showing improved survival.

Brachytherapy via the GliaSite

Significantly more user-friendly way to deliver brachytherapy to the brain

In an attempt to overcome these issues, an intracavitary balloon applicator was developed (GliaSite). This novel inflatable-balloon catheter system is designed specifically to be placed in the tumor bed of malignant brain tumors following their surgical resection. Iotrex (liquid ^{125}I therapy solution) is then infused in the balloon, resulting in localized irradiation of the tumor bed. The use of a *single* intracavitary applicator positioned inside the resection cavity during the initial surgery in place of an interstitial-seed implant removes the need for additional invasive procedures and the need for multiple puncture sites (up to 20).

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Significantly improved dose delivery vs. conventional brachytherapy

The balloon containing Iotrex is placed in direct contact with the resection-cavity wall, providing a dose distribution that is highly conformal with the target tissue around the cavity. Iotrex delivers in a single application the same radiation dose that requires implantation of multiple (up to 125) radioactive seeds. The distribution properties of Iotrex preclude "hot spots." In fact, in comparative testing with ^{125}I seed implants, Iotrex delivered via the GliaSite catheter provides a more conformal therapy with no target tissue underdosing, less target tissue overdosing and no healthy tissue 'hot spots'.

Significantly increased patient access

GliaSite is an easier, more practical means of delivering brachytherapy, but it still offers promising survival improvements associated with conventional brachytherapy. Despite demonstrated improvements in survival over the past two decades, conventional brachytherapy is currently available in fewer than 5 centers nationwide due to the complexity of the involved procedures. As evidence of its practicality and effectiveness, the GliaSite RTS is already available in more than 125 centers in the US. The therapy is being adopted on a widespread basis in both academic and community hospitals to treat patients with malignant brain tumors.

b. List of published peer-review articles relevant to the new service or technology.

deGuzman AF, Kearns WT, Shaw EG, et al. Radiation safety issues with high activities of liquid I-125: Techniques and experience. *J Applied Clinical Med Phys.* Vol. 4, No. 2, Spring 2003.

Dempsey JF, Williams JA, Stubbs JB, Patrick TJ, Williamson JF. Dosimetric properties of a novel brachytherapy balloon applicator for the treatment of malignant brain-tumor resection-cavity margins. *Int J Radiat Oncol Biol Phys.* 1998;42(2):421-429.

Dempsey JF, Low DA, Kirov AS, Williamson JF. Quantitative optical densitometry with scanning-laser film digitizers. *Med Phys.* 1999;26:1721-1731.

FraserRW, Limentani SA, Dollar JD, Asher, A. Recurrent primary fibrosarcoma of the brain treated with the GliaSite brachytherapy system: case report. *Surgical Neurology*. 2003;60:566-70.

Monroe JI, Dempsey JF, Dorton JA, et al. Experimental validation of dose calculation algorithms for the GliaSite® RTS, a novel 125I liquid-filled balloon brachytherapy applicator. *Med Phys.* 2001;28(1):73-85.

Stubbs JB, Strickland AD, Frank RK, et al. Biodistribution and dosimetry of aqueous solution containing sodium 3-(125I)iodo-4-hydroxybenzenesulfonate (Iotrex®) for brachytherapy of resected malignant brain tumors. *Cancer Biother Radiopharm.* 2000;15(6):645-656.

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Stubbs JB, Strickland AD, Frank RK, et al. Neurotoxicity of Iotrex®, an aqueous solution for brachytherapy of resected malignant brain tumors. *J Neurosurgery.* Submitted.

Stubbs J, Frankel R, Schultz K, et al. Preclinical evaluation of a novel device for delivering brachytherapy to resected brain tumor cavity margins. *J Neurosurgery.* 96; 335-343, 2002.

Tatter SB, Shaw EG, Rosenblum ML, et al. An inflatable balloon catheter and liquid ^{125}I radiation source (GliaSite Radiation Therapy System) for treatment of recurrent malignant glioma: multi-center safety and feasibility trial. *J Neurosurgery*. 99: 297-303, 2003.

Zimmerman BE, Cessna JT, and Dorton JA. Experimental investigation of dose calibrator response for ^{125}I brachytherapy solutions contained in 5 mL plastic syringes and 2 mL conical glass v-vials as a function of filling mass. *Med Phys.* 2002;29(7):1547-1555.